REMARKS

Entry of the Amendment and reconsideration of the rejection of claims in view of the following Remarks is respectfully requested.

Claim 52 has been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of this claim in one or more continuation applications.

Claims 30, 38, 43 and 50-51 have been amended. Claims 30 and 43 have been amended to clarify the claims. Claim 38 has been amended to correct an obvious grammatical error. Claim 50 has been amended, the support for which can be found at page 97, lines 20-26. Claim 51 has been amended to provide antecedent basis. No new matter is added by the amendments.

Applicants have amended the specification to update the priority information.

Withdrawn Rejections

Applicants acknowledge the withdrawal of the rejection of claims 41-55 under 35 U.S.C. 112, second paragraph. Applicants also acknowledge the withdrawal of the rejection of claims 41 and 42 under 35 U.S.C. 112, first paragraph.

Double Patenting

Applicants acknowledge the provisional rejection of claims 30-49 under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 30-51 of copending Application No. 09/863,693. Applicants request that the Examiner hold this rejection in abeyance until notice of allowable subject matter.

Applicants acknowledge the provisional rejection of claims 30-49 under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 47-63 of copending Application No. 09/520,130. Applicants request that the Examiner hold this rejection in abeyance upon notice of allowable subject matter.

Applicants acknowledge the provisional rejection of claims 30-49 under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1-29 of copending Application No. 10/143,437. Applicants request that the Examiner hold this rejection in abeyance upon notice of allowable subject matter.

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Written Description

Claims 30-42 have been rejected under 35 U.S.C. §112 second paragraph, as allegedly lacking written description. The Applicants traverse this rejection.

The Examiner contends that the specification only teaches the use of the same light chain in all binding domains in the multispecific antibody. Applicants traverse this rejection.

The fundamental factual inquiry in whether the claims are sufficiently described "is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed." *MPEP 2163 I.B.* Sufficient written description exists for a claim limitation if one of skill in the art can immediately discern the limitation from reading the original specification. *Waldemar Link, GmbH & Co. v. Osteonics Corp.*, 31 USPQ2d 1855 (Fed Cir. 1994). The specification need not, however, describe *ipsis verbis* what is recited in the claims; rather, the claim limitations may be supported in the specification through express, implicit, or inherent disclosure. *MPEP 2163 I.B.* Furthermore, Applicants need not disclose in detail what is conventional or well known to one of ordinary skill in the art. *MPEP 2163 II.A.3(a).* "If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." *Id.* It is the Examiner who bears the burden of "providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed." *MPEP 2163.III.A.*

Claims 30-42 are directed to methods of preparing a multispecific antibody comprising a first polypeptide and at least one additional polypeptide, wherein the polypeptides comprise a binding domain comprising a heavy and a light chain, wherein the light chains of the first and additional polypeptides each have three CDR regions, have at least 98% sequence identity to one another, and only differ from one another at amino acid positions outside of the CDR regions. Applicants submit that one of skill in the art at the time of filing would have clearly understood from reading the specification that Applicants were in possession of these claimed methods at the time of filing.

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The Examiner contends, however, that the present specification does not contemplate multispecific antibodies comprising light chains having even 1 amino acid difference between them, because the specification allegedly only discloses comparing light chains to identify a single common light chain for use in a multispecific antibody.

The Applicants respectfully disagree, and submit that the specification does disclose the use of light chains having less than 100% identity, for example, having at least 98% identity. As stated in the previous Response, the specification discloses two light chains that have 98% sequence identity and differ by two residues outside of the antigen binding CDRs (page 97, line 24 to page 98, line 3. For example, in Figure 4, the light chain sequences have been aligned and the differences shown between the light chains. The specification states that these amino acid changes may have little or no effect on antigen binding (page 97, lines 26-27). The specification concludes that, while the sequence similarity of these light chains makes them candidates for the common light chain of the invention, in an alternative embodiment "according to the invention, such light chains having 98-99% sequence identity with the light chain of a prospective paired scFv (Ax1.78, for example), *may be substituted with the paired light chain and retain binding specificity*" (page 97, line 28 through page 98, line 3) (emphasis added). Applicants submit that one of skill in the art would understand that this embodiment is an alternative to using these light chains as the common light chain and that they each may be substituted for the paired light chain in a scFv specific for example, Ax1.78, and retain binding specificity for that antigen. Therefore, the present specification teaches that light chains having at least 98% sequence identity can be utilized in multispecific antibodies, without having an effect on antigen binding.

For example, if one of skill in the art reading the specification wanted to create a multispecific antibody comprising anti-Ax1.78 and anti-Rse specificity, they could do so by using the Ax1.78 light chain as a common light chain. Alternatively, in accord with the description in the specification, the Ax1.78 light chain could be substituted with the Rse.04 light chain and paired with Ax1.78 heavy chain, and the Rse.04 light chain could be substituted with Ax1.78 light chain and paired with the Rse.04 heavy chain. As discussed in the specification, such pairings would retain antigen binding specificity for Ax1.78 and Rse.04. Since each light chain could also pair with its corresponding heavy chain, there is no mispairing of the light chains. The statement at page 97, line 26, to page 98, line 4, with regard to amino acids changes

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making no difference in antigen specificity coupled with the indication that any of the light chains could be substituted for the paired light chains indicates that light chain variable domains according to the invention are interchangeable with one another demonstrated by several examples as shown in Fig. 4.

Moreover, Applicants further submit the specification contemplated using scFv having different specificities to prepare multispecific antibodies or antigen binding fragments thereof. See the specification at pages 24-25, wherein the specification indicates the first and second polypeptides can include antibody variable domain polypeptides. In addition, Example 4 describes the use of scFv library and variable domain sequences from such a library to prepare a bispecific antibody. See page 97, line 29, to page 101, line 5.

Thus, Applicants submit one of skill in the art reading the specification would understand the specification to provide written description for claims 30-42.

Claims 50 and 53-55 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description. The Examiner contends that the claims should recite that the common light chain differs only outside of the CDRs. Although the Applicants do not agree with the propriety of this rejection, in order to expedite prosecution, claim 50 now recites that the common light chain has at least 98% sequence identity to a variable domain of a light chain of a first antibody and/or at least one additional antibody, and only differs from the first and at least one additional antibody at amino acid positions outside of the CDR regions. Withdrawal of the rejection is requested.

35 U.S.C. 112, second paragraph

Claims 51-52 were rejected under 35 U.S.C. 112, second paragraph for lack of antecedent basis. Claim 51 has been amended to provide antecedent basis. Claim 52 has been cancelled rendering the rejection moot. Withdrawal of the rejection is requested.

Claim Objections

Claim 52 was objected to as failing to further limit the subject matter of claims 50 and 51. Claim 52 has been cancelled rendering the rejection moot. Withdrawal of the rejection is requested.

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Interview

The Applicants hereby request an interview with the Examiner and her supervisor to discuss any remaining rejections. The Examiner is requested to telephone the undersigned Applicants' representative to schedule the interview.

Summary

Applicants submit that the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative if prosecution may be assisted thereby.

Respectfully submitted,

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